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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,103	03/29/2001	Robert Abramowitz	TN17US(2548)	3256
23914	7590	01/28/2004	EXAMINER	
STEPHEN B. DAVIS			OWENS JR, HOWARD V	
BRISTOL-MYERS SQUIBB COMPANY			ART UNIT	
PATENT DEPARTMENT			PAPER NUMBER	
P O BOX 4000			1623	
PRINCETON, NJ 08543-4000			DATE MAILED: 01/28/2004	

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/821,103

### Applicant(s)

ABRAMOWITZ ET AL.

### Examiner

Howard V Owens

### Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11/3/2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 000. 6) ☐ Other:

### **DETAILED ACTION**

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

#### **Response to Restriction/Election Requirement**

Applicant's election with traverse of Group I, claims 1-25 and Species 1 is acknowledged, upon reconsideration, Groups I –III will be examined together.

#### **Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-34 are rejected under 35 U.S.C. § 103 as being unpatentable over Lin et al., U.S. Patent No. 4,978,655 and Ullah et al., U.S. Patent No. 6,607,747.

Claim 1 is drawn to extruded-spheronized beadlets comprising stavudine, a spheronizing agent, and a quantity of magnesium stearate sufficient to stabilize stavudine against degradation during the extrusion-spheronization process.

Dependent claims 2-14 are drawn to modification of the beadlets with an antiadherent such as magnesium stearate, microcrystalline cellulose

Claim 15 is the same as the composition set forth in claim 1; however, it contains a diluent. Dependent claims of 16-18 are drawn to the use of diluents such as corn starch, manitol and lactose. Dependent claim 19 is drawn to the use of a film former, polymeric barrier material and plasticizer.

Claims 21-30 are drawn to the compositions of either 1, 15 or 19 with an additional retroviral agent. Specifically didanosine in accordance with the species election of 11/03/2003.

Claims 31-34 are drawn to forming stavudine beadlets by formation of a wet mass of stavudine, extrusion and spheronizing the extrudate.

Lin teaches the formation of stavudine (d4T) in a composition with common pharmaceutical excipients —such as magnesium stearate, carboxymethyl cellulose and cellulose derivatives, diluents, protective matrices and polymeric substances for sustained delivery (col. 4, lines 10-43). Lin however does not specifically teach an extruded spheronized form nor the addition of didanosine. Ullah adequately bridges the nexus between Lin and the instant claims as it teaches the use of a pharmaceutical composition comprising an extruded spheronized (beadlet) containing the claimed plasticizers, coatings and carboxymethylcellulose binders for stability and modification of the dissolution profile (as well as beadlet formation) wherein the medicament may comprise didanosine or like acid labile compounds (col. 2., line 35 - col. 5, line 12; see also col. 5, line 55 – col. 6, line 16).

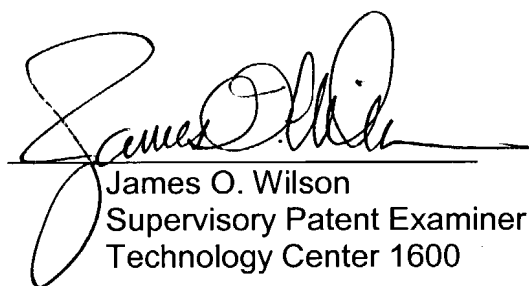
It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to form stavudine as a beadlet wherein various binders and excipients are used to add stability during processing and administration.

One of skill in the art would have been motivated to form stavudine as an extruded spheronized beadlet given that the prior art teaches that these spheronized beadlets

Art Unit: 1623

allow for modification of the dissolution profile when administered and reduce the degradation of acid labile compounds, wherein didanosine and stavudine are exemplary of these compounds.

Howard V. Owens  
Patent Examiner  
Art Unit 1623



James O. Wilson  
Supervisory Patent Examiner  
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.